

**Amendments to the Specification:**

At page 3, please replace lines 30-36 with the following paragraph:

*Figure 1 is Figures 1A-D* are a schematic of the generation of *Msh5* null mice. *Figure 1A* depicts the gene targeting strategy. *Figure 1B* is a depiction of a Southern blot of tail DNA digested with *NsiI*. DNA analysis of 606 offspring from heterozygote matings produced 184 *Msh5*<sup>+/+</sup>, 275 *Msh5*<sup>+/-</sup> and 147 *Msh5*<sup>-/-</sup>, confirming the Mendelian transmission of the mutant allele. *Figure 1C* is a depiction of a Northern blot of RNA from *Msh5*<sup>+/+</sup> and *Msh5*<sup>-/-</sup> mouse testes with different probes. *Figure 1D* is a depiction of a Western blot of proteins from male testes with anti-MSH5 antibody.

At page 4, please replace lines 1-14 with the following paragraph:

*Figure 2 Figures 2A-G* depicts the disruption of spermatogenesis in *Msh5*<sup>-/-</sup> males. *Figure 2A* is a depiction of the mRNA expression of *Msh5* (upper panel) and actin (lower panel) in testes from wild-type males between the ages of 8 days and 29 days, and in adult wild-type and *Msh5*<sup>-/-</sup> males. *Figures 2B-E* is are a depiction of H&E stained sections of adult testis from wild-type (*B, D*) and *Msh5*<sup>-/-</sup> (*C, E*) males showing loss of spermatocytes beyond zygonema in *Msh5*-deficient males. Le, Leydig cell; S, Sertoli cell; A, type A spermatogonia; B, type B spermatogonia; PL, pre-Leptotene; L, Leptotene spermatocyte; Z, Zygote spermatocyte; P, Pachytene spermatocyte; RS, round spermatid; ES, elongated spermatid; Sp, spermatozoa. *Figures 2F,G* is are a depiction of the immunolocalization of germ cells using anti-GCNA1 antibody (red immunoreactive protein against a light blue counterstain) on sections from wild-type (*F*) and *Msh5*<sup>-/-</sup> (*G*) testes from 29 day old males showing abundant spermatocytes, spermatids and spermatozoa in wild-type testes and a few GCNA1-positive cells in the MSH5-deficient testes. (For *B* and *C*, scale bar = 100 µm; for *D-G*, scale bar = 25 µm).

At page 4, please replace lines 15-24 with the following paragraph:

*Figure 3 Figures 3A-H* depicts the progressive depletion of germ cells in *Msh5*<sup>-/-</sup> males during development. *Figures 3A, B, E, F, I, J* is are a depiction of germ cell immunolocalization using the anti-GCNA1 antibody of testes from wild-type (*A, E-I*) and *Msh5*<sup>-/-</sup> (*B, F-J*) males showing the rapid depletion of germ cells from day 17pp onwards in *Msh5*-deficient mice in

contrast to the increasing density and variety of spermatogenic cells in the seminiferous tubules of *Msh5*<sup>+/+</sup> males. *Figures 3C, D, G, H, K, L* is are a depiction of TUNEL staining of testes from wild-type (*C, G, K*) and *Msh5*<sup>-/-</sup> males (*D, H, L*) showing continuous apoptosis from day 17 pp onwards compared to the very low level of apoptosis in tubules from wild-type males over the same time frame. (Scale bar = 100 µm.)

At page 4, please replace lines 25-30 with the following paragraph:

*Figures 4A-C* depicts the disruption of meiosis prior to synapsis in *Msh5* spermatocytes. *Figures 4 A-C* is are a depiction of silver-stained spermatocytes from wild-type (*A*) and *Msh5*<sup>-/-</sup> (*B,C*) testes showing complete failure of pairing (*B*) or some partial pairing (*C*) in the absence of MSH5. Arrowheads in panel (*C*) indicate chromosomes exhibiting partial pairing. Note that many of these chromosomes appear to be unequally paired.

Please replace the paragraph starting at page 4, line 31 and ending at page 5, line 3 with the following paragraph:

*Figures 5A-F* depicts the loss of oocytes and subsequent ovarian degeneration in *Msh5*<sup>-/-</sup> females. *Figures 5A,B* depicts ovaries from day 3 pp wild-type (*A*) and *Msh5*<sup>-/-</sup> (*B*) females showing oocytes stained with GCNA1. *Figure 5Ce* depicts the entire ovary from a day 25 pp *Msh5*<sup>-/-</sup> female (H&E staining) containing only 3 follicles and degenerating tissue. *Figure 5D,E* is a depiction of H&E stained ovaries from adult wild-type (*D*) and *Msh5*<sup>-/-</sup> females (*E*) showing complete loss of oocytes and ovarian architecture in the absence of *Msh5*. B, ovarian bursa; Ov, oviduct. In all cases, scale bar = 200 µm. *Figure 5F* is a depiction of the expression of ZP3 and Actin in ovaries of wild-type and *Msh5*<sup>-/-</sup> ovaries on day 25 pp and in the adult.

At page 5, please replace lines 4-14 with the following paragraph:

*Figures 6A-J* shows that the disruption of oogenesis in *Msh5*<sup>-/-</sup> females leads to a failure of folliculogenesis. *Figures 6A-D* depicts ovaries from e18 wild-type (*A,B*) and *Msh5*<sup>-/-</sup> (*C,D*) embryos showing oogonia stained with anti-GCNA1 (*A,C*) or H&E localization of meiotic chromosome detail (*C,D*). *Figures 6E-H* depicts GCNA1 localization of oocytes in ovaries from day 3 pp wild-type (*E,F*) and *Msh5*<sup>-/-</sup> (*G,H*) females. Arrowheads indicate pachytene oocytes (punctate red staining of nucleus compared to solid red staining of pre-pachytene oocytes), arrows indicate the appearance of the earliest primordial follicles. *Figures 6I, and 6J, is* are a depiction of GCNA1 localization of oocytes in ovaries from day 6pp wild-type (*I,J*) females

(overstained to stain oocytes in meiotic arrest). Arrows indicate primordial follicles; o, oocyte. For *A, C, E, G, and I* scale bar = 100  $\mu\text{m}$ ; for *B, D, F, H, and J* scale bar = 25  $\mu\text{m}$ .

At page 19, please replace lines 1-4 with the following:

increased apoptosis (see Figure 3*A, B, C, D*). By day 23 pp, the tubules of wild-type mice contain round spermatids (see Figure 3*E, G*). In contrast, elevated levels of apoptosis in *Msh5*<sup>-/-</sup> tubules leads to continued germ cell attrition (see Figure 3*F, H*) and by adulthood, almost the entire spermatogenic cell population is lost (see Figure 3*I-L*).